

IN THE CLAIMS:

Please amend the claims as follows:

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a 40. (amended) An agent for use against a living organism, said agent comprising an oligodeoxynucleotide in a stabilized form to inhibit degradation by said living organism and having a nucleotide sequence substantially complementary to a base sequence of at least a portion of messenger ribonucleic acid coding for a protein vital to said organism's viability and capable of hybridization with said messenger ribonucleic acid so as to substantially block translation of said base sequence and inhibit synthesis of said protein after introducing into said organism.

✓ In claim 41, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

✓ In claim 42, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

✓ In claim 43, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

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a 45. (amended) An agent for use in controlling synthesis of a protein, said agent comprising an oligodeoxynucleotide in a stabilized form to inhibit degradation and having a nucleotide sequence substantially complementary to a base sequence of at least a portion of messenger ribonucleic acid coding for said protein and capable of hybridization with said messenger ribonucleic acid so as to substantially block translation of said base sequence and inhibit synthesis of said protein after introducing into said organism.

In claim 46, line 2, delete "oligonucleotide" and insert

✓ therefore --oligodeoxynucleotide.--

✓ In claim 47, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

49. (amended) A therapeutic agent useful in controlling synthesis of a protein from an organism, said agent comprising a stabilized oligodeoxynucleotide, the sequence of which is derived from ribonucleic or deoxyribonucleic acid isolated from said organism, wherein said sequence is substantially complementary to a portion of messenger ribonucleic acid coding for said protein and capable of hybridization with said messenger ribonucleic acid so as to substantially block translation of said base sequence and inhibit synthesis of said protein after introducing into said organism.

✓ In claim 51, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

✓ In claim 52, line 2, delete "oligonucleotide" and insert therefore --oligodeoxynucleotide.--

Add the following claims:

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R126 53
--84. A method of developing oligodeoxyribonucleotide therapeutic agents for use in in vivo inhibition of the synthesis of one or more targeted proteins in a cell without substantially inhibiting the synthesis of non-targeted proteins, comprising the steps of:

determining the base sequence of an organism's messenger ribonucleic acid, said base sequence coding for at least a portion of said protein targeted for inhibition;

synthesizing an oligodeoxyribonucleotide, the nucleotide sequence of which is substantially complementary to at least a portion of said base sequence and capable of hybridization with

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Contd

said messenger ribonucleic acid base sequence coding for at least a portion of a protein targeted for inhibition so as to substantially block translation of said base sequence and inhibit synthesis of said targeted protein after introducing into the cells of said organism, and

at least a portion of said oligodeoxyribonucleotide being a more stable form in order to limit degradation in vivo.--

R126 ⁵⁴--~~85~~. The method of claim ⁵³~~84~~, wherein said more stable form is a phosphotriester form.--

R126 ⁵⁵--~~86~~. The method of claim ⁵³~~84~~, wherein said oligodeoxyribonucleotide comprises at least 14 nucleotides.--

R126 ⁵⁶--~~87~~. The method of claim ⁵³~~84~~, wherein said oligodeoxyribonucleotide comprises about 23 nucleotides.--

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cont.

R126 ⁵⁷--~~88~~. The method of claim ⁵³~~84~~, wherein the order of said base sequence is determined from ribonucleic acid or deoxyribonucleic acid coding for said targeted protein prior to synthesizing the oligodeoxyribonucleotide.--

R126 ⁵⁸--~~89~~. The method of claim ⁵³~~84~~, wherein the order of said base sequence is determined from messenger ribonucleic acid coding for said targeted protein prior to synthesizing said oligodeoxyribonucleotide.--

R126 ⁵⁹--~~90~~. The method of claim ⁵³~~84~~, wherein the order of said base sequence is determined from said targeted protein prior to synthesizing said oligodeoxyribonucleotide.--

R126 ⁶⁰--~~91~~. The method of claim ⁵³~~84~~, wherein said oligodeoxyribonucleotide is synthesized chemically.--

R126 ⁶¹--~~92~~. A method of developing oligodeoxyribonucleotide

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therapeutic agents for use in in vivo inhibition of the synthesis of one or more targeted proteins in a cell without substantially inhibiting the synthesis of non-targeted proteins, comprising the steps of:

determining the base sequence of an organism's messenger ribonucleic acid, said base sequence coding for at least a portion of said protein targeted for inhibition;

synthesizing an oligodeoxyribonucleotide, the nucleotide sequence of which is substantially complementary to at least a portion of said base sequence and capable of hybridization with said messenger ribonucleic acid base sequence coding for at least a portion of said protein targeted for inhibition so as to substantially block translation of said base sequence and inhibit synthesis of said targeted protein after introducing into the cells of said organism;

at least a portion of said oligodeoxyribonucleotide being a stabilized form in order to limit degradation in vivo;

cross hybridizing said oligodeoxyribonucleotide against messenger ribonucleic acid from at least one species different from said organism; and

selecting that fraction of the oligoribonucleotide which does not so hybridize so as to increase the specificity of the selected oligodeoxyribonucleotide to messenger ribonucleic acid unique to said organism.--

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as cont.
R126 ⁶² --93. A method of selectively inhibiting in vivo synthesis of one or more specific targeted proteins without substantially inhibiting the synthesis of non-targeted proteins, comprising the steps of:

synthesizing an oligodeoxyribonucleotide having a nucleotide sequence substantially complementary to at least a portion of the base sequence of messenger ribonucleic acid coding for said targeted protein;

at least a portion of said oligodeoxyribonucleotide being in the form of a phosphotriester to limit degradation in vivo;